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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,534	06/10/2005	Wayne D. Frasch	21926	4137
7590	05/12/2010		EXAMINER	
Peter I. Bernstein, Scully, Scott, Murphy & Presser, P.C. Suite 300 400 Garden City Plaza Garden City, NY 11530			SHAW, AMANDA MARIE	
			ART UNIT	PAPER NUMBER
			1634	
			MAIL DATE	DELIVERY MODE
			05/12/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/538,534	Applicant(s) FRASCH ET AL.
	Examiner Amanda Shaw	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 05 April 2010.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 40,42-47,49-54 and 56-60 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 40,42-47,49-54, and 56-60 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO/SB/06)
 Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____
 5) Notice of Informal Patent Application
 6) Other: _____

DETAILED ACTION

1. This action is in response to the amendment filed April 5, 2010. This action is made FINAL.

Claims 40, 42-47, 49-54, 56-60 are currently pending.

Claims 40, 42, 47, 49, 54, 56, 57, and 60 have been amended.

Terminal Disclaimer

2. The terminal disclaimer filed on April 5, 2010 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on US Application No 10/582,820 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Withdrawn Rejections

3. The rejection made under 35 USC 112 1st paragraph (new matter) in section 2 of the Office Action of January 6, 2010 is withdrawn in view of the amendments made to claim 60.

The double patenting rejection made in section 10 of the Office Action of January 6, 2010 is withdrawn in view of the terminal disclaimer filed over Application 10/582,820.

Claim Objections

4. Claim 54 is objected to for having a typographical error. Specifically the "A" in the word attaching should not be capitalized.

Claims 57 and 58 are objected to because they depend on a claim that has been cancelled.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejections have all been previously presented however some have been modified slightly to address the amendments made to the claims.

6. Claims 40, 42-45, 47 and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yasuda et al (Nature 2001) in view of Sonnichsen (Physical Review Letter Pub 1/2002) (as evidenced by Mock (Nano Letters Pub 4/2002)) and in further view of Pettingell et al (US Patent 6449088 Filed 1993).

Regarding Claims 40 and 42-45 Yasuda teaches a method of detecting motion in nanoscale structures. Yasuda teaches providing a molecular structure having a rotating arm, wherein the molecular structure is an F1-ATPase enzyme (Abstract). Yasuda further teaches attaching a nanoparticle (i.e. a 40 nm bead) to the rotating arm of the molecular structure so that the nanoparticle rotates with the rotating arm of the molecular structure (See Fig 1). Yasuda further teaches that bead rotation was imaged by laser dark field microscopy and only light scattered by the bead was detected (Page 898 and Fig 1). Thus Yasuda teaches a step of exposing a light to the nanoparticle wherein the nanoparticle scatters light. Further Yasuda teaches that it was desirable to observe rotational motion of F1-ATPase in order to investigate the magnitudes, speeds, and timings of the substeps that make up a full rotation (page 898).

Yasuda does not teach a method wherein the nanoparticle has a first surface and a second surface wherein the first surface has greater area than the second surface (clm 40). Yasuda does not teach that the first surface of the nanoparticle scatters a first polarized wavelength of the light when the nanoparticle is in a first position and the second surface of the nanoparticle scatters a second polarized wavelength of light when the nanoparticle is in a second position (clm 40). Yasuda does not teach a method wherein the nanoparticle is rod shaped (clm 40). Yasuda does not teach a method

wherein the rod shaped nanoparticle is a gold nanorod (clm 42). Additionally Yasuda does not teach a method wherein the first polarized wavelength of light is longer than the second polarized wavelength of light (clm 43). Finally Yasuda does not teach a method wherein the first polarized wavelength of light is red light and the second polarized wavelength of the light is green light (clm 44).

However Sonnichsen teaches methods that use gold nanoparticles that are in the shape of rods. The rods have diameters of $b= 15-25$ nm along the two short axes and lengths of up to $a= 100$ nm (page 2, col 1). Thus Sonnichsen teaches a nanoparticle that has a first and second surface wherein one surface has a greater area than the other surface. Sonnichsen teaches that the long axis resonance can be examined by using excitation light polarized along the long axis and that the short axis resonance spectra can be examined by using excitation light polarized along the short axis (page 2, col 2). As evidenced by Mock it is a property of the nanorod that when light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). Specifically Figure 3e shows color images of a silver/gold/nickel coded nanowire, illuminated with light polarized along the long axis. The gold portion gives off red light when illuminated with light polarized along the long axis. Figure 3f is the same silver/gold/nickel coded nanowire as in 3e, but it is illuminated with light polarized along the short axis. The gold portion gives off green light when illuminated with light polarized along the short axis. As such it is a property of nanorods that they have a first

surface that scatters a first polarized wavelength of light when the nanorod is in a first position relative to the light source (i.e., when the light is polarized along the long axis) and a second surface that scatters a second polarized wavelength of light when the nanorod is in a second position relative to the light source (i.e., when the light is polarized along the short axis).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda by using a gold nanorod as suggested by Sonnichsen (and evidenced by Mock). In the instant case, Sonnichsen teaches that rods appear as bright in the microscopic measurement as spheres of much larger volume (page 077402-4, col 1). Since Yasuda was concerned about having a particle that was large enough to scatter enough light to create an image that can be captured but small enough so as to not impede rotation one of skill in the art would have been motivated to modify the method of Yasuda by using a gold nanorod. One of skill in the art would have also recognized that it was advantageous to use gold nanorods to observe rotational motion because gold nanorods have two different surfaces. As evidenced by Mock it is a property of the nanorod that when light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). Thus one of skill in the art would have been motivated to modify Yasuda by using a gold nanorod so that rotational motion could be detected by observing alternating flashes of red and green light. Additionally Sonnichsen teaches that they found a drastic reduction

Art Unit: 1634

of the plasmon dephasing rate in nanorods as compared to nanospheres and that nanorods compared to nanospheres showed much weaker radiation damping. These findings result in relatively high light scattering efficiencies and large local field enhancement factors, making nanorods interesting for a range of optical applications (page 4, col 2). In addition, the courts have found that changes in shape are obvious (*In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966)). Thus, a nanorod is an obvious variation of a nanosphere. See MPEP 2144.04 [R-6] IV B. Further the claimed invention would have been obvious because the substitution of a nanosphere for a nanorod would have yielded predictable results (i.e., the ability to observe alternating first and second wavelengths of light as the nanorods move from one position to the next position) to one of ordinary skill in the art at the time of the invention.

Additionally it is noted that the combined teachings of Yasuda and Sonnichsen (as evidenced by Mock) do not teach a step of filtering the first and second wavelengths of light through a polarizing filter (clm 40).

However Pettingell discloses using polarizing microscopes which use polarizers to look at anisotropic materials (nanorods are anisotropic because they have a first and second axis) (Column 3, lines 10-15). The polarizing filters are used to separate the first and second wavelengths of light generated by anisotropic materials.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda and Sonnichsen (as evidenced by Mock) by using the polarizer of Pettingell. Polarizers were well known in the art at the time of the invention for looking at anisotropic materials as

demonstrated by Pettingell. Thus after the substitution of a non anisotropic material (i.e., the nanobead of Yasuda) for an anisotropic material (i.e., the nanorod of Sonnichsen) it would have been obvious to one of skill in the art at the time of the invention to look at other observation techniques available particularly ones that were used for looking at anisotropic materials since nanorods are anisotropic. One would have been motivated to use a polarizing filter because they allow for the separation of colors such as red and green that are produced when light is first polarized along the long axis of a gold nanorod and then polarized along the short axis of a gold nanorod. Further all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Regarding Claims 47 and 49-52 Yasuda teaches a method of detecting motion in nanoscale structures. Yasuda teaches attaching a nanoparticle (i.e. a 40 nm bead) to the rotating arm of an F1-ATPase enzyme so that the nanoparticle rotates with the rotating arm of the F1-ATPase enzyme (See Fig 1). Yasuda further teaches that bead rotation was imaged by laser dark field microscopy and only light scattered by the bead was detected (Page 898 and Fig 1). Thus Yasuda teaches a step of exposing a light to the nanoparticle wherein the nanoparticle scatters light. Further Yasuda teaches that it was desirable to observe rotational motion of F1-ATPase in order to investigate the magnitudes, speeds, and timings of the substeps that make up a full rotation (page 898).

Yasuda does not teach a method wherein the nanoparticle has a first surface and a second surface wherein the first surface has greater area than the second surface (clm 47). Yasuda does not teach exposing light to a first surface of the nanoparticle to scatter a first polarized wavelength of the light and exposing light to a second surface of the nanoparticle to scatter a second polarized wavelength of light (clm 47). Yasuda does not teach a method wherein the nanoparticle is rod shaped (clm 47). Further Yasuda does not teach a method wherein the rod shaped nanoparticle is a gold nanorod (clm 49). Additionally Yasuda does not teach a method wherein the first polarized wavelength of light is longer than the second polarized wavelength of light (clm 50). Finally Yasuda does not teach a method wherein the first polarized wavelength of light is red light and the second polarized wavelength of the light is green light (clm 51).

However Sonnichsen teaches methods that use gold nanoparticles that are in the shape of rods. The rods have diameters of $b= 15-25$ nm along the two short axes and lengths of up to $a= 100$ nm (page 2, col 1). Thus Sonnichsen teaches a nanoparticle that has a first and second surface wherein one surface has a greater area than the other surface. Sonnichsen teaches that the long axis resonance can be examined by using excitation light polarized along the long axis and that the short axis resonance spectra can be examined by using excitation light polarized along the short axis (page 2, col 2). As evidenced by Mock it is a property of the nanorod that when light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when light is polarized along the short axis of the gold nanowire it

produces green light (which has a wavelength of about 510 nm) (See Fig 3).

Specifically Figure 3e shows color images of a silver/gold/nickel coded nanowire, illuminated with light polarized along the long axis. The gold portion gives off red light when illuminated with light polarized along the long axis. Figure 3f is the same silver/gold/nickel coded nanowire as in 3e, but it is illuminated with light polarized along the short axis. The gold portion gives off green light when illuminated with light polarized along the short axis. As such it is a property of nanorods that they have a first surface that scatters a first polarized wavelength of light when the nanorod is in a first position relative to the light source (i.e., when the light is polarized along the long axis) and a second surface that scatters a second polarized wavelength of light when the nanorod is in a second position relative to the light source (i.e., when the light is polarized along the short axis).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda by using a gold nanorod as suggested by Sonnichsen (and evidenced by Mock). In the instant case, Sonnichsen teaches that rods appear as bright in the microscopic measurement as spheres of much larger volume (page 077402-4, col 1). Since Yasuda was concerned about having a particle that was large enough to scatter enough light to create an image that can be captured but small enough so as to not impede rotation one of skill in the art would have been motivated to modify the method of Yasuda by using a gold nanorod. One of skill in the art would have also recognized that it was advantageous to use gold nanorods to observe rotational motion because gold nanorods have two different

surfaces. As evidenced by Mock it is a property of the nanorod that when light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). Thus one of skill in the art would have been motivated to modify Yasuda by using a gold nanorod so that rotational motion could be detected by observing alternating flashes of red and green light. Additionally Sonnichsen teaches that they found a drastic reduction of the plasmon dephasing rate in nanorods as compared to nanospheres and that nanorods compared to nanospheres showed much weaker radiation damping. These findings result in relatively high light scattering efficiencies and large local field enhancement factors, making nanorods interesting for a range of optical applications (page 4, col 2). In addition, the courts have found that changes in shape are obvious (*In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966)). Thus, a nanorod is an obvious variation of a nanosphere. See MPEP 2144.04 [R-6] IV B. Further the claimed invention would have been obvious because the substitution of a nanosphere for a nanorod would have yielded predictable results (i.e., the ability to observe alternating first and second wavelengths of light as the nanorods move from one position to the next position) to one of ordinary skill in the art at the time of the invention.

Additionally it is noted that the combined teachings of Yasuda and Sonnichsen (as evidenced by Mock) do not teach a step of filtering the first and second wavelengths of light through a polarizing filter (clm 47).

However Pettingell discloses using polarizing microscopes which use polarizers to look at anisotropic materials (nanorods are anisotropic because they have a first and second axis) (Column 3, lines 10-15). The polarizing filters are used to separate the first and second wavelengths of light generated by anisotropic materials.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda and Sonnichsen (as evidenced by Mock) by using the polarizer of Pettingell. Polarizers were well known in the art at the time of the invention for looking at anisotropic materials as demonstrated by Pettingell. Thus after the substitution of a non anisotropic material (i.e., the nanobead of Yasuda) for an anisotropic material (i.e., the nanorod of Sonnichsen) it would have been obvious to one of skill in the art at the time of the invention to look at other observation techniques available particularly ones that were used for looking at anisotropic materials since nanorods are anisotropic. One would have been motivated to use a polarizing filter because they allow for the separation of colors such as red and green that are produced when light is first polarized along the long axis of a gold nanorod and then polarized along the short axis of a gold nanorod. Further all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

7. Claims 54 and 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yasuda et al (Nature 2001) in view of Sonnichsen (Physical Review Letter Pub 1/2002) (as evidenced by Mock (Nano Letters Pub 4/2002)).

Regarding Claims 54 and 56-59 Yasuda teaches a method of detecting motion. Yasuda teaches attaching a nanoparticle (i.e. a 40 nm bead) to the rotating arm of an F1-ATPase enzyme so that the nanoparticle rotates with the rotating arm of the F1-ATPase enzyme (See Fig 1). Thus Yasuda teaches attaching a nanoparticle to a rotating portion (rotating arm) of a base structure (the F1-ATPase). Yasuda further teaches that bead rotation was imaged by laser dark field microscopy and only light scattered by the bead was detected (Page 898 and Fig 1). Thus Yasuda teaches a step of exposing a light to the nanoparticle wherein the nanoparticle scatters light. Further Yasuda teaches that it was desirable to observe rotational motion of F1-ATPase in order to investigate the magnitudes, speeds, and timings of the substeps that make up a full rotation (page 898).

Yasuda does not teach a method wherein an anisotropic nanoparticle is used (clm 54). Yasuda does not teach exposing light to the anisotropic nanoparticle to scatter first polarized and second polarized wavelengths of the light (clm 54). Yasuda does not teach a method wherein the anisotropic nanoparticle is rod shaped (clm 54). Further Yasuda does not teach a method wherein the rod shaped anisotropic nanoparticle is a gold nanorod (clm 56). Yasuda does not teach that the anisotropic nanoparticle has a first surface and a second surface wherein the first surface has greater area than the second surface (clm 57). Additionally Yasuda does not teach a method wherein the first

Art Unit: 1634

polarized wavelength of light is longer than the second polarized wavelength of light (clm 58). Finally Yasuda does not teach a method wherein the first polarized wavelength of light is red light and the second polarized wavelength of the light is green light (clm 59).

However Sonnichsen teaches methods that use gold nanoparticles that are in the shape of rods. The rods have diameters of $b= 15\text{--}25$ nm along the two short axes and lengths of up to $a= 100$ nm (page 2, col 1). Thus Sonnichsen teaches a nanoparticle that has a first and second surface wherein one surface has a greater area than the other surface. Sonnichsen teaches that the long axis resonance can be examined by using excitation light polarized along the long axis and that the short axis resonance spectra can be examined by using excitation light polarized along the short axis (page 2, col 2). As evidenced by Mock it is a property of the nanorod that when light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). Specifically Figure 3e shows color images of a silver/gold/nickel coded nanowire, illuminated with light polarized along the long axis. The gold portion gives off red light when illuminated with light polarized along the long axis. Figure 3f is the same silver/gold/nickel coded nanowire as in 3e, but it is illuminated with light polarized along the short axis. The gold portion gives off green light when illuminated with light polarized along the short axis. As such it is a property of nanorods that they have a first surface that scatters a first polarized wavelength of light when the nanorod is in a first

position relative to the light source (i.e., when the light is polarized along the long axis) and a second surface that scatters a second polarized wavelength of light when the nanorod is in a second position relative to the light source (i.e., when the light is polarized along the short axis).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda by using a gold nanorod as suggested by Sonnichsen (and evidenced by Mock). In the instant case, Sonnichsen teaches that rods appear as bright in the microscopic measurement as spheres of much larger volume (page 077402-4, col 1). Since Yasuda was concerned about having a particle that was large enough to scatter enough light to create an image that can be captured but small enough so as to not impede rotation one of skill in the art would have been motivated to modify the method of Yasuda by using a gold nanorod. One of skill in the art would have also recognized that it was advantageous to use gold nanorods to observe rotational motion because gold nanorods have two different surfaces. As evidenced by Mock it is a property of the nanorod that when light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). Thus one of skill in the art would have been motivated to modify Yasuda by using a gold nanorod so that rotational motion could be detected by observing alternating flashes of red and green light. Additionally Sonnichsen teaches that they found a drastic reduction of the plasmon dephasing rate in nanorods as compared to nanospheres and that

nanorods compared to nanospheres showed much weaker radiation damping. These findings result in relatively high light scattering efficiencies and large local field enhancement factors, making nanorods interesting for a range of optical applications (page 4, col 2). In addition, the courts have found that changes in shape are obvious (*In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966)). Thus, a nanorod is an obvious variation of a nanosphere. See MPEP 2144.04 [R-6] IV B. Further the claimed invention would have been obvious because the substitution of a nanosphere for a nanorod would have yielded predictable results (i.e., the ability to observe alternating first and second wavelengths of light as the nanorods move from one position to the next position) to one of ordinary skill in the art at the time of the invention.

8. Claims 46 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yasuda et al (Nature 2001) in view of Sonnichsen (Physical Review Letter Pub 1/2002) (as evidenced by Mock (Nano Letters Pub 4/2002)), and Pettingell et al (US Patent 6449088 Filed 1993) as applied to claims 40 and 47 above and in further view of Felder (US Patent 6232066).

The teachings of Yasuda, Sonnichsen (as evidenced by Mock), and Pettingell are presented above.

As discussed above Yasuda teaches a method comprising attaching a nanoparticle (i.e. a 40 nm bead) to the rotating arm of an F1-ATPase so that the nanoparticle rotates with the rotating arm of the F1-ATPase (See Fig 1). As shown in Figure 1 the bead was attached to the F1-ATPase through streptavidin/biotin binding.

The combined references do not teach a method which includes a step of disposing a detection DNA strand between the nanoparticle and the molecular structure, wherein the detection DNA strand hybridizes with a target DNA strand, if the target DNA strand matches the detection DNA strand, to form a structural link between the molecular structure and the nanoparticle.

However Felder teaches a method for DNA detection. Felder teaches a method wherein a linker oligonucleotide is attached to anchor (col 1 line 66 to col 2 line 3). Felder teaches that the anchor can be a protein (col 7, line 7) and in the instant case the F1-ATPase is being interpreted as the anchor since it is a protein. Felder further teaches that the linker oligonucleotide contains a sequence that is specific for the target to be detected (col 1 line 66 to col 2 line 3). Felder teaches that if the target is present a portion of the target will hybridize to the linker oligonucleotide and another portion of the target will hybridize to a detection oligonucleotide comprising a label (col 1 line 66 to col 2 line 3). Thus Felder teaches a method wherein the linker oligonucleotide, the target oligonucleotide, and the detection oligonucleotide form a structural link between the anchor and the label.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda, Sonnichsen (as evidenced by Mock), and Pettingell by using a linker oligonucleotide, a target oligonucleotide, and a detection oligonucleotide to attach the nanoparticle (i.e., the label) to the F1-ATPase (i.e., the anchor) as suggested by Felder. One of skill in the art would have been motivated to use a linker oligonucleotide, a target oligonucleotide, and

a detection oligonucleotide to attach the nanoparticle (i.e., the label) to the F1-ATPase (i.e., the anchor) rather than streptavidin/biotin binding for the benefit of being able to detect hybridization. This modification allows one to detect hybridization because if the target is present the nanoparticle (i.e., label) would be attached to F1-ATPase (i.e., anchor) and rotation of the nanoparticle could be observed and would indicate the presence of the target. On the other hand if the target was not present the nanoparticle (i.e., label) would not attach to the F1-ATPase (i.e., anchor) and rotation of the nanoparticle could not be observed and would indicate the absence of the target.

9. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yasuda et al (Nature 2001) in view of Sonnichsen (Physical Review Letter Pub 1/2002) (as evidenced by Mock (Nano Letters Pub 4/2002)), Felder (US Patent 6232066), and Greenberg (US Patent 5305139).

Yasuda teaches a method of detecting motion in nanoscale structures. Yasuda teaches providing a molecular structure having a rotating arm, wherein the molecular structure is an F1-ATPase enzyme (Abstract). Yasuda further teaches attaching a nanoparticle (i.e. a 40 nm bead) to the rotating arm of the molecular structure so that the nanoparticle rotates with the rotating arm of the molecular structure (See Fig 1). Yasuda further teaches that bead rotation was imaged by laser dark field microscopy. Specifically Yasuda teaches that a laser beam was introduced into a dark field condenser to illuminate the specimen obliquely (page 903 col 1 and Fig 1). Thus Yasuda teaches providing light from a fixed location, altering the path of the light from

the fixed location to create and oblique angle, and exposing the light from the altered path onto the nanoparticle. Yasuda then teaches that light scattered by beads was collected with a $\times 1000$ objective with its diaphragm (also known as an iris) set to NA ~ 1.1 to block the direct ray (page 903, col 1 Fig 1). Thus Yasuda teaches providing an iris which passes the scattered light and blocks unscattered light. Further Yasuda teaches that it was desirable to observe rotational motion of F1-ATPase in order to investigate the magnitudes, speeds, and timings of the substeps that make up a full rotation (page 898).

Yasuda does not teach a method wherein the nanoparticle has a first axis and a second axis wherein the first axis has a great length than the second axis. Yasuda does not teach that the first axis of the nanoparticle scatters a first wavelength of the light when the nanoparticle is in a first position and the second axis of the nanoparticle scatters a second wavelength of light when the nanoparticle is in a second position. Yasuda does not specifically state that the light is white light. Yasuda does not teach detecting alternating first and second wavelength which indicate motion of the nanoparticle and the molecular structure.

However Sonnichsen teaches methods that use gold nanoparticles that are in the shape of rods. The rods have diameters of $b= 15-25$ nm along the two short axes and lengths of up to $a= 100$ nm (page 2, col 1). Thus Sonnichsen teaches a nanoparticle that has a first and second axis wherein one axis has a length greater than the length of the other axis. Sonnichsen teaches that the long axis resonance can examined by using excitation light polarized along the long axis and that the short axis resonance

spectra can be examined by using excitation light polarized along the short axis (page 2, col 2). As evidenced by Mock it is a property of the nanorod that when white light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when white light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). Specifically Figure 3e shows color images of a silver/gold/nickel coded nanowire, illuminated with white light polarized along the long axis. The gold portion gives off red light when illuminated with white light polarized along the long axis. Figure 3f is the same silver/gold/nickel coded nanowire as in 3e, but it is illuminated with white light polarized along the short axis. The gold portion gives off green light when illuminated with white light polarized along the short axis. As such it is a property of nanorods that they have a first axis that scatters a first polarized wavelength of light when the nanorod is in a first position relative to the light source (i.e., when the light is polarized along the long axis) and a second axis that scatters a second polarized wavelength of light when the nanorod is in a second position relative to the light source (i.e., when the light is polarized along the short axis).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda by using a gold nanorod as suggested by Sonnichsen (and evidenced by Mock). In the instant case, Sonnichsen teaches that rods appear as bright in the microscopic measurement as spheres of much larger volume (page 077402-4, col 1). Since Yasuda was concerned about having a particle that was large enough to scatter enough light to create an image

that can be captured but small enough so as to not impede rotation one of skill in the art would have been motivated to modify the method of Yasuda by using a gold nanorod. One of skill in the art would have also recognized that it was advantageous to use gold nanorods to observe rotational motion because gold nanorods have two different surfaces. As evidenced by Mock it is a property of the nanorod that when light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). Thus rotational motion of the nanoparticle and the molecular structure can be detected by observing alternating flashes of red and green light (which have different wavelengths). Additionally Sonnichsen teaches that they found a drastic reduction of the plasmon dephasing rate in nanorods as compared to nanospheres and that nanorods compared to nanospheres showed much weaker radiation damping. These findings result in relatively high light scattering efficiencies and large local field enhancement factors, making nanorods interesting for a range of optical applications (page 4, col 2). In addition, the courts have found that changes in shape are obvious (*In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966)). Thus, a nanorod is an obvious variation of a nanosphere. See MPEP 2144.04 [R-6] IV B. Further the claimed invention would have been obvious because the substitution of a nanosphere for a nanorod would have yielded predictable results (i.e., the ability to observe alternating first and second wavelengths of light as the nanorods move from one position to the next position) to one of ordinary skill in the art at the time of the invention.

Additionally it is noted that the combined teachings of Yasuda and Sonnichsen (as evidenced by Mock) do not teach a method which includes a step of disposing a detection DNA strand between the nanoparticle and the molecular structure, wherein the detection DNA strand hybridizes with a target DNA strand such that if the target DNA strand matches the detection DNA strand they form a structural link between the molecular structure and the nanoparticle causing the nanoparticle to rotate.

However Felder teaches a method for DNA detection. Felder teaches a method wherein a linker oligonucleotide is attached to anchor (col 1 line 66 to col 2 line 3). Felder teaches that the anchor can be a protein (col 7, line 7) and in the instant case the F1-ATPase is being interpreted as the anchor since it is a protein. Felder further teaches that the linker oligonucleotide contains a sequence that is specific for the target to be detected (col 1 line 66 to col 2 line 3). Felder teaches that if the target is present a portion of the target will hybridize to the linker oligonucleotide and another portion of the target will hybridize to a detection oligonucleotide comprising a label (col 1 line 66 to col 2 line 3). Thus Felder teaches a method wherein the linker oligonucleotide, the target oligonucleotide, and the detection oligonucleotide form a structural link between the anchor and the label.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda and Sonnichsen (as evidenced by Mock) by using a linker oligonucleotide, a target oligonucleotide, and a detection oligonucleotide to attach the nanoparticle (i.e., the label) to the F1-ATPase (i.e., the anchor) as suggested by Felder. One of skill in the art would have been

Art Unit: 1634

motivated to use a linker oligonucleotide, a target oligonucleotide, and a detection oligonucleotide to attach the nanoparticle (i.e., the label) to the F1-ATPase (i.e., the anchor) rather than streptavidin/biotin binding for the benefit of being able to detect hybridization. This modification allows one to detect hybridization because if the target is present the nanoparticle (i.e., label) would be attached to F1-ATPase (i.e., anchor) and rotation of the nanoparticle could be observed and would indicate the presence of the target. On the other hand if the target was not present the nanoparticle (i.e., label) would not attach to the F1-ATPase (i.e., anchor) and rotation of the nanoparticle could not be observed and would indicate the absence of the target.

Additionally it is noted that the combined teachings of Yasuda, Sonnichsen (as evidenced by Mock) and Felder do not teach a step of providing a polarizing filter which is aligned only to the first and second wavelengths of the light wherein the polarizing filter blocks light not aligned with the filter, processing the first and second wavelengths of light from the polarizing filter through optical equipment to separate the first and second wavelengths of light into first and second channels respectively.

However Greenberg teaches a method wherein polarizing filters are used. Greenberg teaches that the filters may be complementary color filters (such as red and green) of either the absorption or dichroic type (col 11 lines 15-30 Fig 2). Thus Greenberg teaches a step of providing a polarizing filter which is aligned only to the first and second wavelengths of the light wherein the polarizing filter blocks light not aligned with the filter. Greenberg further teaches polarizing filters may be used to separate beams of light so that the illumination of each beam enters a different one of the eye

pieces (col 11 line 65 to col 12 line 7). Thus Greenberg teaches processing the first and second wavelengths of light from the polarizing filter through optical equipment to separate the first and second wavelengths of light into first and second channels respectively.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda, Sonnichsen (as evidenced by Mock) and Felder by using a polarizing filter as suggested by Greenberg. Polarizers were well known in the art at the time of the invention for looking at anisotropic materials as demonstrated by Greenberg. Thus after the substitution of a non anisotropic material (i.e., the nanobead of Yasuda) for an anisotropic material (i.e., the nanorod of Sonnichsen) it would have been obvious to one of skill in the art at the time of the invention to look at other observation techniques available particularly ones that were used for looking at anisotropic materials since nanorods are anisotropic. One would have been motivated to use a polarizing filter because they allow for the separation of colors such as red and green that are produced when light is first polarized along the long axis of a gold nanorod and then polarized along the short axis of a gold nanorod. Further all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 40-59 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,989,235 in view of Sonnichsen (Physical Review Letter Pub 1/2002) (as evidenced by Mock (Nano Letters Pub 4/2002)) and Pettingell et al (US Patent 6449088 Filed 1993).

Although the conflicting claims are not identical, they are not patentably distinct from each other. In the instant case both sets of claims are drawn to a method of detecting motion in nano scale structures. Both methods require a molecular structure having a rotating arm such as a F1 ATPase. Both methods require attaching a nanoparticle to the rotating arm so that the nanoparticle rotates with the rotating arm of the molecular structure. Further both sets of claims include a step of disposing a DNA

detection strand between the nanoparticle and the molecular structure wherein the DNA detection strand hybridizes with a target DNA strand if the target DNA strand matches the DNA detection strand.

The instant claims are different from the conflicting claims because they require a nanoparticle that has a first surface and a second surface wherein the first surface has a great area than the second surface (in other words an anisotropic nanoparticle). Dependent claims further state that the nanoparticle is a gold nanorod. Additionally the claims are different because they require exposing light to the nanoparticle wherein a first surface of the nanoparticle scatters a first polarized wavelength of light when the nanoparticle is in a first position and a second surface of the nanoparticle scatter a second polarized wavelength of light when the nanoparticle is in a second position. However Sonnichsen teaches methods that use gold nanoparticles that are in the shape of rods (page 2, col 1). Sonnichsen teaches that the long axis resonance can examined by using excitation light polarized along the long axis and that the short axis resonance spectra can be examined by using excitation light polarized along the short axis (page 2, col 2). As evidenced by Mock it is a property of the nanorod that when white light is polarized along the long axis of a gold nanorod it produces red light (which has a wavelength of about 650 nm) and when white light is polarized along the short axis of the gold nanowire it produces green light (which has a wavelength of about 510 nm) (See Fig 3). As such it is a property of nanorods that they have a first axis that scatters a first polarized wavelength of light when the nanorod is in a first position relative to the light source (i.e., when the light is polarized along the long axis) and a second axis that

Art Unit: 1634

scatters a second polarized wavelength of light when the nanorod is in a second position relative to the light source (i.e., when the light is polarized along the short axis). Accordingly, it would have been obvious to modify the method of US Patent 6989235 by using a gold nanorod. One of skill in the art would have been motivated to modify the patent based on the teaching is Sonnichsen that rods appear as bright in the microscopic measurement as spheres of much larger volume (page 077402-4, col 1). In addition, the courts have found that changes in shape are obvious (*In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966)). Thus, a nanorod is an obvious variation of a nanosphere. See MPEP 2144.04 [R-6] IV B.

The instant claims are also different from the conflicting claims because they require filtering the first and second wavelengths of the light through a polarizing filter to detect rotation motion by observing alternating first and second wavelengths of light. However Pettingell discloses using polarizing microscopes which use polarizers to look at anisotropic materials (nanorods are anisotropic because they have a first and second axis) (Column 3, lines 10-15). The polarizing filters are used to separate the first and second wavelengths of light generated by anisotropic materials. Accordingly, it would have been obvious to modify the method of US Patent 6989235 by using the polarizer of Pettingell. Polarizers were well known in the art at the time of the invention for looking at anisotropic materials as demonstrated by Pettingell. Thus after the substitution of a non anisotropic material (i.e., the nanobead of Yasuda) for an anisotropic material (i.e., the nanorod of Sonnichsen) it would have been obvious to one of skill in the art at the time of the invention to look at other observation techniques

available particularly ones that were used for looking at anisotropic materials since nanorods are anisotropic.

Response to Arguments

12. In the response filed on April 5, 2010 the Applicants state that the claimed invention has solved a long-felt but unsolved need that has been widely accepted by the scientific community. They state that the inventors and particularly Dr Wayne Frasch have been recognized as making a significant contribution in the field by other renowned experts in the field. The Applicants then cite several papers.

This argument has been fully considered and is not persuasive. Applicants are reminded that MPEP 716.01(c) states that objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, **solution of a long-felt need**, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. In the instant case the arguments of counsel with respect to the Applicants claim of solving a long felt need cannot take the place of evidence in the record. This should not be construed as an invitation for providing additional declarations or affidavits. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) *Timeliness*. Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. *In re Rothermel*, 276 F.2d 393, 125 USPQ 328

(CCPA 1960). Affidavits and declarations submitted under **37 CFR 1.132** and other evidence traversing rejections are considered timely if submitted:

- (1) prior to a final rejection,
- (2) before appeal in an application not having a final rejection, *
- (3) after final rejection **>, but before or on the same date of filing an appeal, upon a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented in compliance with **37 CFR 1.116(e)**; or
- (4) after the prosecution is closed (e.g., after a final rejection, after appeal, or after allowance) if applicant files the affidavit or other evidence with a request for continued examination (RCE) under **37 CFR 1.114** in a utility or plant application filed on or after June 8, 1995; or a continued prosecution application (CPA) under **37 CFR 1.53(d)** in a design application.

Additionally Applicants argue that claim 60 is allowable because the cited art does not teach each and every element. In particular they argue that the references fail to disclose disposing a detection DNA strand between the nanoparticle and the molecular structure, wherein the detection DNA strand hybridizes with a target DNA strand such that if the target DNA strand matches the detection DNA strand they form a structural link between the molecular structure and the nanoparticle causing the nanoparticle to rotate. Regarding Felder they state that no target matching DNA linkage between a rotating molecular motor and nanoparticle suitable for causing the nanoparticle to rotate is discussed. Further they argue that Felder requires a surface

comprising multiple spatially discrete regions, at least two of which are substantially identical, however this is not required in the present invention.

This argument has been fully considered and is not persuasive. In the instant case Applicants are reminded that this is a 103 rejection and is based on a combination of references. In the instant case Yasuda teaches attaching a nanoparticle to a rotating arm of an F1-ATPase via a biotin/streptavidin linkage. The biotin/streptavidin linkage is considered to be a structural link between the molecular structure and the nanoparticle which would cause the nanoparticle to rotate when the molecular structure rotated. The Office Action acknowledges that Yasuda does not teach attaching a nanoparticle to a rotating arm of an F1-ATPase via a detection DNA strand. However Felder teaches a method wherein a linker oligonucleotide is attached to anchor (col 1 line 66 to col 2 line 3). Felder teaches that the anchor can be a protein (col 7, line 7) and in the instant case the F1-ATPase is being interpreted as the anchor since it is a protein. Felder further teaches that the linker oligonucleotide contains a sequence that is specific for the target to be detected (col 1 line 66 to col 2 line 3). Felder teaches that if the target is present a portion of the target will hybridize to the linker oligonucleotide and another portion of the target will hybridize to a detection oligonucleotide comprising a label (col 1 line 66 to col 2 line 3). Thus Felder teaches a method wherein the linker oligonucleotide, the target oligonucleotide, and the detection oligonucleotide form a structural link between the anchor and the label. Thus all of the claimed limitations have been taught and the rejection is maintained.

Regarding the double patenting rejection made over US Patent 6,989,235 the Applicants argue that the patent uses nanospheres or beads and not a nanorod.

This argument has been fully considered and is not persuasive. The claims are rejected on the ground of nonstatutory *obviousness-type* double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,989,235 in view of Sonnichsen (Physical Review Letter Pub 1/2002) (as evidenced by Mock (Nano Letters Pub 4/2002)) and Pettingell et al (US Patent 6449088 Filed 1993). In the instant case the fact that the US Patent uses nanospheres or beads is irrelevant because Sonnichsen teaches nanorods which are rod shaped nanoparticles. For this reason the rejection is maintained.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634

/Stephen Kapushoc/
Primary Examiner, Art Unit 1634